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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/393,590	09/09/99	MOYER E	00211-US-NEW

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EXAMINER	
DEVI,S	
ART UNIT	**PAPER NUMBER**
1645	8

DATE MAILED: 10/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/393,590	Moyer et al.
Examiner	**Group Art Unit**
S. Devi, Ph.D.	1645

☒ Responsive to communication(s) filed on *Aug 1, 2000* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-53* is/are pending in the application.

Of the above, claim(s) *29-53* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5 & 7.*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Change of Art Unit Location

1) Effective 20 June 2000, the Art Unit location of the instant application in the US PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1645.

Election

2) Acknowledgment is made of Applicants' election, without traverse, of invention I (claims 1-28) filed 08/01/00 (paper no. 6), in response to the restriction requirement mailed 07/10/00 (paper no. 4). As requested by Applicants, method claims are retained as pending claims in accordance with M.P.E.P 821.04. The restriction requirement is hereby made FINAL.

Status of Claims

3) Claims 1-58 are pending in the instant application.

Claims 1-28 have been elected via the election filed 08/01/00.

Claims 29-58 have been withdrawn from consideration as being directed to non-elected inventions. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1-28 are under examination. An Action on the Merits for these claims is issued in the instant Office Action (paper no. 8).

Priority

4) The instant application claims domestic priority to the provisional application, SN 60/099,870, filed 09/11/98.

Information Disclosure Statements

5) Acknowledgment is made of Applicants' Information Disclosure Statements filed 08/01/00 and 08/23/00 (paper no. 5 and 7). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 8).

In the papers filed 08/01/00 and 08/23/00 (paper no. 5 and 7), Applicants state the following:

> A copy of a search report issued by the European Patent Office in related case PCT/US99/20912 is enclosed. The references cited therein in the listing on form PTO/SB/08A.

However, the search report submitted to the Office is not of PCT/US99/20912, but of PCT/US93/05973. Applicants are asked to submit the search report related to case PCT/US99/20912 and submit the references cited therein via a new PTO-1449, if Applicants desired consideration of those references.

Specification

6) Instant specification is objected to because on page 1, line 23, the word "toxoiing" is misspelled. Correction is requested.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

7) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

8) Claims 8-12 and 21-25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 9 depends from claim 8. Claims 9 and 8 are confusing in the inconsistent and/or incorrect recitations: "serotype" and "Type" with regard to the botulinum toxin. A review of the art suggests that the term "serotype" is used to refer to the bacterium, *Clostridium botulinum*, whereas the term "type" is used to refer to its toxin. See for example, page 2, lines 10-12 of the patent EP 0 593 176 A2. It is suggested that Applicants use the correct and the consistent recitation.

(b) Claim 22 depends from claim 21. Claims 22 and 21 are confusing in the inconsistent and/or incorrect recitations: "serotype" and "Type" with regard to the botulinum toxin. A review of the art suggests that the term "serotype" is used to refer to the bacterium, *Clostridium botulinum*, whereas the term "type" is used to refer to its toxin. See for example, page 2, lines 10-12 of the patent EP 0 593 176 A2. It is suggested that Applicants use the correct and the consistent recitation.

(c) Claims 10-12 and 23-25 which depend directly or indirectly from claims 8 and 21 respectively, are also rejected under 35 U.S.C. § 112, second paragraph, because of the confusing

and/or incorrect recitations in the base claim(s) identified above in subparagraphs (a) and (b).

Rejection(s) under 35 U.S.C § 112, First Paragraph

9) Claims 1-8, 12-22 and 25-28 are rejected under 35 U.S.C § 112, first paragraph, because the specification while being enabling for a liquid pharmaceutical botulinum type B toxin formulation comprising a succinate buffer and human serum albumin with a pH of 5.6, which is stable for 6 months to 12 months at a temperature of 0-30 degrees centigrade, does not reasonably provide enablement for such a pharmaceutical formulation comprising a botulinum toxin other than type B comprising any liquid buffer including the recited phosphate, phosphate-citrate and succinate buffers, as claimed in a broad sense.

Instant claims are analyzed based on the *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, Example 1 of the disclosure shows that a type B botulinum toxin liquid formulation comprising a liquid succinate buffer with a pH of 5.6 remains potent or retains stability for periods varying between 0 to 30 months when stored at 5 degrees centigrade (see Table 2). The specification further provides evidence for a type B botulinum toxin formulation, which remains stable for six months at 25 degrees centigrade (see Table 3). However, the instant specification does not enable, or it lacks evidence for any other liquid botulinum toxin formulation other than type B which remains stable for six months or one year when formulated in any buffer of pH 5-6 and when stored at a temperature of 0-10 or 10-30 degrees centigrade, as claimed. This is important, because preservation properties of different types of botulinum toxin are not identical. For instance, Prevot *et al.* (*Ann. Pasteur Inst.* 2-20, 1993 - Applicants' IDS) teach that toxin E sometimes behaves like groups A and B botulinum toxins and sometimes like groups C

and D toxins with regard to the preservation at +4 degree centigrade. Prevot *et al.* further teach that, for botulinum C and D toxins, the preservation is independent of the pH. The art also reflects the batch-to-batch inconsistency in the stability of different botulinum toxins when stored at +4 degree centigrade at a pH between 5-6 (see pages 9 and 10). Therefore, due the art-recognized dissimilarity between the preservation properties of different botulinum toxins, the unpredictable stability, the lack of evidence in the instant disclosure that is commensurate in scope, the lack of sufficient and/or specific guidance, the breadth of claims and the quantity of experimentation necessary, undue experimentation would have been required by one of ordinary skill in the art to reproducibly practice the full scope of the invention as claimed. The instant claims are viewed as not meeting the provisions of 35 U.S.C. § 112, first paragraph.

Objection(s)

10) Claims 8 and 21 are objected to for the following reason:

(a) For clarity, in claims 8 and 21, it is suggested that Applicants insert the word --of-- after the second occurrence of "botulinum toxin".

Remarks

11) Claims 1-28 stand rejected.

12) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week.

13) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD
S. Devi
Patent Examiner
October 2000